

Synthesis, Characterization and Invitro Antimicrobial Investigation of Some Transition Metal Complexes with the Schiff Base of Aromatic Aldehyde

RICHA KOTHARI^{1*} and BRAJRAJ SHARMA²

Department of Engg. Chemistry
Institute of Technology and Management, Gwalior, India

ABSTRACT

Transition metal complexes of Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) with a bidentate ligand, bis (2-Pyridyl Carboxylaldehyde) ethylene diamine derived from the condensation of 2-Pyridyl carboxylaldehyde and ethylene diamine was synthesized. Characterization has been done on the basis of analytical, conductance and magnetic data, infrared, ^1H NMR, electronic spectral data. From analytical data, the stoichiometry of the complexes has been found to be 1:2 (metal: ligand). According to these data, we propose an octahedral geometry for metal (II) complexes. The ligand and metal complexes were screened for their physiological activities against *E.coli*, *Staphylococcus aureus*, *Bacillus subtilis* and *Salmonella typhi*.

Keywords: Schiff base, Metal complexes, Antibacterial activity.

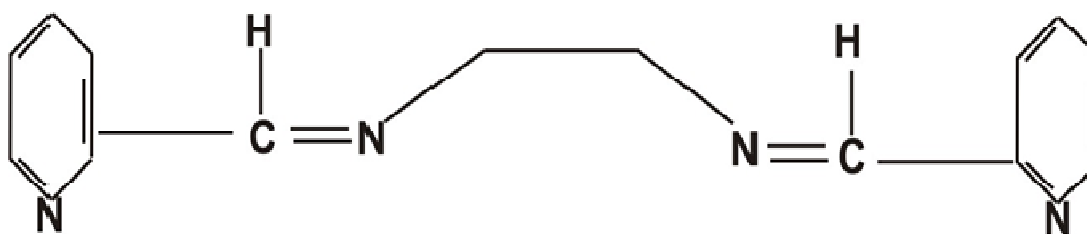
INTRODUCTION

Schiff bases and their coordination compounds have gained importance recently¹⁻⁵ because of their application as models in biological, biochemical, analytical, antimicrobial system⁶, anticancer, antibacterial⁷, antifungal⁸ activities and anti tumor activity⁹⁻¹⁰. They have been studied extensively as a class of ligands¹¹⁻¹³ and are known to coordinate with metal ions through the azomethine nitrogen atom. The synthesis of transition metal complexes with Schiff base ligands are extensively studied due to

synthetic flexibility, selectivity and sensitivity towards a variety of metal atoms¹⁴. They are found useful in catalysis, in medicine as antibiotics and anti-inflammatory agents and in the industry as anticorrosion¹⁵⁻²¹. Literature is abundant on physico-chemical properties of various Symmetrical Schiff bases and chelates with their Pyridine, 2, 2'-bipyridine and 1, 10-phenanthroline adducts²²⁻²⁶, while comparatively little is known on asymmetric Schiff base transition metal complexes. In the present paper we describe the behaviour of the bidentate aromatic Schiff base ligands

with various transition metal (II) ions. The spectral properties of the ligand and their complexes have been measured and the results are discussed in order to obtain information on the stereochemistry of the compounds in the solid state. All these compounds with the ligands (fig.1) are new, being reported for the first time. The structures of all these complexes have been

investigated by using elemental analysis, FTIR, ^1H NMR, UV-VIS, Magnetic susceptibility and conductivity measurements. Antibacterial activities were determined as MICs values using the micro dilution broth method against gram-positive bacteria; staphylococcus aureus and Bacillus subtilis and gram-negative bacteria Salmonella typhi and Escherichia coli.



bis(2-Pyridyl carboxylaldehyde) ethylene diamine

MATERIAL AND METHODS

(2.1) Physical measurements

All reagents were supplied by Merck and were used without further purification. Melting points were determined in a Electro thermal 9200. ^1H NMR spectra in CDCl_3 and DMSO were recorded on NMR spectrophotometer. The IR spectra (nujol/KBr) were recorded in the range 400-4000 cm^{-1} by KBr pellet using Perkin-Elmer 457 spectrophotometer. Conductance was measured in DMF at room temperature using a Digital conductivity bridge. The UV-Visible spectra in CH_3OH were recorded on a shimadzu UV 1800 spectrophotometer. The metal contents were determined gravimetrically.

(2.2) Synthesis of Schiff base ligands

The Schiff base ligand was prepared by equimolar mixture of derivatives aldehydes (2mmol) and the diamine (1mmol) in methanol for 3 hr. TLC Examination suggested the complete conversion of the starting materials to the Schiff base. Upon cooling, the obtained crystalline precipitates were filtered, washed with ethanol and recrystallized from absolute ethanol and finally dried. They are colorless, and light yellow crystalline solids, stable at normal condition and soluble in DMSO, DMF; poorly soluble in benzene and water.

(2.3) Synthesis of transition metal (II) complexes

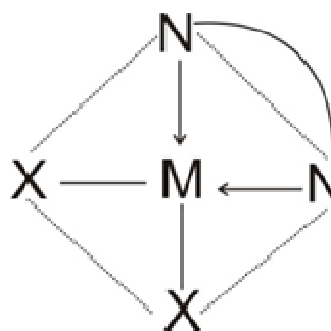
All complexes are prepared by the following general method. A hot methanoic solution of the corresponding metal (II) salt was mixed with a hot methanoic solution of the Schiff base ligand in molar ratio 1:2 respectively. The reaction mixture was refluxed on a water bath for ~ 2 hours. On cooling the reaction mixture at room temperature the colored complexes precipitated out in each case. The complexes were filtered out, recrystallized, washed with methanol and dried over P_4O_{10} under vacuum.

(2.4) Procedure for antibacterial activity

The invitro antibacterial activity of the free ligands and their complexes were tested against the gram positive bacteria: *S. aureus*, and *Bacillus subtilis* and gram negative bacteria *E. coli* and *Salmonella typhi*. Minimum inhibitory concentrations (MICs) were determined by the micro dilution broth method following the procedures recommended by the National committee for clinical laboratory standards²⁷⁻²⁸. MICs were defined as the lowest concentrations of compounds which inhibit the growth of micro organisms. All tests were performed in Nutrient Broth (NB) dissolved in DMSO which lacked anti bacterial activity against any of the test bacteria. The micro plates were incubated at 37° C and read visually after 24 hr for MICs²⁹. The results were recorded according to the presence and absence of growth.

RESULTS AND DISCUSSION

The transition metal (II) complexes with bidentate aromatic Schiff base ligands were prepared in good yield by stirring stoichiometric amounts of metal (II) chloride and bidentated aromatic Schiff base ligand. Analytical data and some Physical properties of the Bidentate Schiff base ligands and their metal complexes are listed in table 1



Schematic representation of metal complex

The complexes were characterized by the usual methods: elemental analysis, FTIR, 1H NMR, absorption electronic spectroscopy. The complexes are stable in air and light and are soluble in organic solvents such as DMF and DMSO. Elemental analysis ($\pm 0.5\%$ for C, H, and N) and molar conductance data (Less than $60 \Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$ in acetone) suggest the complexes to be non-electrolyte with composition of $MX_2\text{-SB}^{30}$.

Structural Interpretation

Infrared spectra

The infrared spectra of the complexes taken in the region $400\text{-}4000 \text{ cm}^{-1}$ were compared with those of the free ligands. There are some significant changes between the metal (II)

Table 1. The Physical and analytical data of the ligand and complexes

Compound	Color/yield (%)	m.p. (°C)	Calculation (found %)				Λ_m^* ($\Omega^{-1}\text{cm}^2\text{mol}^{-1}$)	$\mu_{\text{eff}}(\text{BM})$
			C	H	N	M		
Schiff base	Yellow/(75)	210°C	32.4 (32.7)	3.2 (3.5)	10.8 (10.9)	---	-----	--
[CoL ₂ Cl ₂]	Brown/(72)	230°C	38.2 (38.4)	3.0 (3.2)	9.6 (9.9)	9.03 (9.00)	22	3.88
[NiL ₂ Cl ₂]	Green/(60)	160 °C	29.4 (29.6)	2.6 (2.8)	11.4 (11.5)	8.9 (8.8)	24	3.10
[CuL ₂ Cl ₂]	Brown/ (78)	200 °C	35.4 (35.9)	2.2 (2.6)	10.4 (10.4)	9.57 (9.55)	28	1.88
[ZnL ₂ Cl ₂]	Yellow/ (80)	180 °C	29.4 (29.5)	3.0 (3.1)	14.4 (14.2)	8.5 (8.6)	34	---
[CdL ₂ Cl ₂]	Yellow/ (75)	170 °C	32.4 (32.9)	2.2 (2.5)	10.2 (14.4)	15.82 (15.81)	32	---
[HgL ₂ Cl ₂]	White/ (70)	220 °C	38.6 (38.7)	2.2 (2.5)	14.8 (14.4)	37.2 (37.5)	36	---

*in 10^{-3} M DMF solution at room temperature

complexes and their free ligands for chelation as expected. The IR bands observed at $1610\text{--}1660\text{ cm}^{-1}$ of all the ligands and the complexes are assigned to ν C=N vibration³¹.

The ligand bands around 1610 cm^{-1} (C=N) shifted to $1635\text{--}1660\text{ cm}^{-1}$ in the complexes due to an increase of bond order on co-ordination³². The bands at $420\text{--}390$ and $344\text{--}210\text{ cm}^{-1}$ in the complexes may be assigned to ν M-N and ν M-Cl modes³³ respectively. The IR spectra of $[\text{ML}_2]\text{Cl}_2$ complexes, the ligands act as a neutral bidentate through the azomethine and carbonyl groups³⁴.

The azomethine band is shifted to lower frequency in all metal complexes, suggesting that this group takes part in coordination. The co-ordination of nitrogen to the metal atom would be expected to

reduce the electron density on the azomethine link and thus cause a shift in the C=N band.

Moreover, in the spectra of the complexes, a considerable negative shift in ν (C=O) are observed indicating a decrease in the stretching force constant of C=O as a consequence of co-ordination through the carbonyl oxygen atom of the free ligands³⁵.

¹H NMR spectra

In NMR spectra of metal (II) complexes we observed a shift of electron density from the ligand to the metal. ¹H NMR spectra of the complexes show all the expected signals. In all the spectra, a singlet corresponding to a single proton is observed in the range δ 9.2, 11.4 ppm, which is attributed to the azo-methine proton ($-\text{HC}=\text{N}$) in metal (II) complexes respectively.

Table2 The Antibacterial activity of the ligand and its complexes

Compound* C*	E. coli	Salmonella typhi	B. subtilis	S. aureus
Schiff base L	++	+	+	+
[CoL ₂ Cl ₂]	++++	+++	+++	++
[Ni L ₂ Cl ₂]	+++	++	++	++
[CuL ₂ Cl ₂]	++++	++	++	++
[ZnL ₂ Cl ₂]	+++	++	++	++
[CdL ₂ Cl ₂]	++	++	++	++
[HgL ₂ Cl ₂]	++	++	++	++

C* = 5 mg/L. Inhibition zone diameter mm (% inhibition) “+, 6-10 (27-45 %); ++10-14 (45-64 %); +++ 14-18 (64-82 %); ++++18-22 % (82-100 %)

The ¹H NMR spectra of the [ML₂]Cl₂ complexes show a negative shift of the signal due to the NH group. This signal is observed at δ 8.0, 11.2 ppm in metal complexes, suggesting that the co-ordination proceeds through the carbonyl oxygen or azomethine nitrogen groups. The downfield shifts of the methyl group signal at 2.4, 2.2 ppm for the metal (II) complexes, support the co-ordination via the azomethine nitrogen. The multi signals within the range δ 8-7.1, 8.3-7.6 ppm are assigned to the aromatic protons of ring in metal (II) complexes respectively.

Electronic spectra

The formation of the metal (II) complexes was also confirmed by UV-VIS spectra. The absorption spectra of the diamagnetic metal (II) complexes were recorded as 10⁻⁴ M CH₃OH solutions in the

range 200-800 nm using a quartz cuvette of 1 cm path length. The complexes show only the charge transfer transitions which can be assigned to charge transfer from the ligand to metal and vice-versa, no d-d transition are expected for d¹⁰ Hg (II) complexes³⁶. When compared complexes with the free ligands values have shifts frequency. The data of the spectra of the metal (II) complexes in CH₃OH solutions are shown that absorption band observed at 275 and 316 nm is attributed to n->π* electronic transition of azomethine group involving the whole conjugation.

Antibacterial activity results of the ligands and complexes

The antibacterial activity of bidentated aromatic Schiff base ligands and their metal (II) complexes were tested against microorganism. The microorganisms

used in the present investigations include bacteria: *Staphylococcus aureus*, *Bacillus subtilis*, *salmonella typhi* and *E.coli*. Minimum inhibitory concentrations (MICs) method was used to determine the antibacterial activity of the synthesized compounds. The diffusion method is simple and routinely used in hospital laboratories; it requires commercial disks, the medium used is Mueller-Hinton agar with 2% of glucose and the diameter of inhibition zone is visually read at 24 hr after incubation at 37°C. The antibacterial activity was estimated on the basis of the size of the inhibition zone formed around the paper disks on the seeded agar plates. Streptomycin was used as a standard. The results are presented in table 2.

Percent inhibition values are relative to the inhibition zone (22 mm) of the most active compound with 100% inhibition. The Schiff base and the complexes exhibited varying degrees of inhibitory effects on the growth of the tested bacteria species. The values reveal that the Schiff base become more effective when coordinated to the metal ions. The biological activity of the complexes follows the order: Co (II) > Ni (II) \approx Cu (II) \approx Zn (II) > Cd (II) \approx Hg (II). Furthermore, the data show that *E. coli* was inhibited to a greater degree by the Co (II) and Cu (II) complexes. In conclusion the complexes prepared with the new Schiff base could reasonable be used for the treatment of some common diseases caused by *E.Coli*.

CONCLUSION

Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) complexes of the Schiff base derived from 2-pyridyl carboxylaldehyde and Ethylenediamine were prepared and characterized. The study reveal that (1) complexes are non-electrolytes (2) Schiff base behaves as a neutral Bidentate ligand and is coordinated to the central metal ion through the azomethine N (3). The metal (II) complexes have octahedral geometry (4). The biological activity of all the complexes is higher that of the free Schiff base ligand and follows the order: Co (II) > Ni (II) \approx Cu (II) \approx Zn (II) > Cd (II) \approx Hg (II). This means that metal chelation significantly affects the antimicrobial behavior of the organic ligand.

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